PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:		(11) International Publication Number:	WO 95/29588
A01N 37/12, 37/44, 43/50, 43/58, 43/60, 47/10, A61K 31/27, 31/50, 31/195, 31/415, 31/495	A1	(43) International Publication Date:	9 November 1995 (09.11.95)
(21) International Application Number: PCT/US (22) International Filing Date: 21 April 1995 ((81) Designated States: AU, CA, F European patent (AT, BE, CH, IE, IT, LU, MC, NL, PT, SE).	I, HU, JP, KR, NZ, PL, DE, DK, ES, FR, GB, GR,
(30) Priority Data: 08/234,089 28 April 1994 (28.04.94) 08/413,742 30 March 1995 (30.03.95)		US US	Published With international search repor	rt.
(71) Applicant: ISP CHEMICALS INC. [US/US]; 116 Avenue, Chatham, NJ 07928-0837 (US).	5 Sumr	nit		
(72) Inventor: MERIANOS, John, J.; 32 Doherty Drive town, NJ 07748 (US).	, Midd	le-		
(74) Agents: MAUE, Marilyn, J. et al.; International Products, 1361 Alps Road, Wayne, NJ 07470 (US	Specia S).	lty		

(54) Title: SYNERGISTIC WATER SOLUBLE PRESERVATIVE COMPOSITIONS OF BIOCIDAL MIXTURES

(57) Abstract

A water soluble preservative admixture of biocidal compounds for addition to commercial use compositions at predetermined use levels, and uniformly distributed therein, to provide long-time synergistic biocidal activity against a wide range of fungi and both gramnegative and gram-positive bacteria, which comprises powders of (a) one or more methylol compounds, or their equivalents, and (b) iodopropynyl alcohol, or its ester, carmabate or ether derivative thereof, in a weight ratio of (a):(b) of 100:1 to 2000:1.

ď,

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
ΑU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgystan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic	SD	Sudan
CG	Congo		of Korea	SE	Sweden
CH	Switzerland	KR	Republic of Korea	SI	Slovenia
CI	Côte d'Ivoire	KZ	Kazakhstan	SK	Slovakia
CM	Сатегоол	LI	Liechtenstein	SN	Senegal
CN	China	LK	Sri Lanka	TD	Chad
CS	Czechoslovakia	LU	Luxembourg	TG	Togo
CZ	Czech Republic	LV	Latvia	TJ	Tajikistan
DE	Germany	MC	Monaco	TT	Trinidad and Tobago
DK	Denmark	MD	Republic of Moldova	UA	Ukraine
ES	Spain	MG	Madagascar	US	United States of America
FI	Finland	ML	Mali	UZ	Uzbekistan
FR	France	MN	Mongolia	VN	Viet Nam
GA	Gabon		-		

SYNERGISTIC WATER SOLUBLE PRESERVATIVE COMPOSITIONS OF BIOCIDAL MIXTURES

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to a water soluble preservative admixture for addition to commercial use formulations to provide long time synergistic biocidal activity therein, and, more particularly, to admixtures of a methylol compound and an iodopropynyl compound, in predetermined weight ratios of 100:1 to 2000:1.

2. Description of the Prior Art

Combinations of antimicrobial agents have been developed in the prior art in order to:

- (1) produce a biochemical synergism;
- (2) broaden the antimicrobial spectrum of activity of each agent;
- (3) increase water solubility for the admixture;
- (4) minimize the toxicity or irritation of a given agent to the host; and
- (5) minimize physical and chemical incompatibilities.

True biological synergism exists when two agents, when combined, require lesser amounts of the agents to bring about the same inhibitory or cidal effect than either single agent alone. While synergistic interaction for two or more antimicrobial agents does produce more than merely an additive effect in the resultant biological activity, in most cases the mechanism of such synergism remains a mystery.

M. Rosen et al., in U.S. Patent 4,844,891, for example, described a preservative admixture of (a) a formaldehyde donor and (b) a halopropynyl compound, in a weight ratio of (a):(b) of 50:1 to 1:1, preferably 30:1 to 2:1, and, most preferably, 20:1 to 10:1, as providing fungicidal activity for 1-3 days in commercial use formulations. However, Rosen observed that when the ratio of (a):(b) in the concentrate exceeded 50:1 (System No. 16 in Table 1, a ratio of 73.33), the preservative composition was ineffective in providing biocidal protection in the use formulations. Thus a relatively large amount of the halopropynyl compound was required by Rosen to provide significant biocidal activity in the use composition. In such admixtures, although the formaldehyde donor is water soluble, the halopropynyl compound is substantially insoluble in water. Therefore it was difficult for Rosen to uniformly distribute his admixture throughout the use composition.

For these and other reasons, it is desired to provide a new and improved water soluble preservative admixture of such biocidal compounds which requires relatively little of the water insoluble and expensive halopropynyl compound, and that also provides effective synergistic protection in use formulations against a wide range of fungi and bacteria at different use levels over a long period of time.

A feature of the present invention is the provision of an admixture concentrate which is water soluble and which therefore can be uniformly distributed in use compositions at a predetermined use level.

Another feature herein is the provision of a preservative admixture which exhibits a long term synergistic biocidal activity against wide range of fungi and both gram-negative and gram-positive bacteria in the use compositions.

Still another feature of this invention is the provision of a water soluble preservative admixture for personal care compositions in the form of a solution, lotion, gel, emulsion, emulsifiable concentrate, suspension, slurry or cream.

These and other objects and features of the invention will be made apparent from the following more particular description of the invention.

SUMMARY OF THE INVENTION

What has been discovered is a water soluble preservative composition for addition to commercial use compositions at predetermined use levels, and uniformly distributed therein, which provides long term synergistic biocidal activity against a wide range of fungi and both gram-negative and gram-positive bacteria. The composition of the invention comprises an admixture of powders of

- (a) a methylol compound, or their equivalent,
- (b) iodopropynyl alcohol, or its ester, carbamate or ether derivative thereof, in a weight ratio of (a):(b) of 100:1 to 2000:1, preferably 200:1 to 500:1.

Commercial use compositions containing about 0.01 to 2% by weight of the composition of the invention also are provided therein. Such use compositions contain an iodopropynyl compound in an amount of about 0.5 to 10 ppm, to provide the desired antifungal activity, and a methylol compound, or equivalent thereof, in an amount of at least 250 ppm, to provide the desired antibacterial activity.

In another embodiment of the invention the composition also includes propylene glycol or 1,3-butylene glycol.

DETAILED DESCRIPTION OF THE INVENTION

The invention is based upon the discoveries that in a predetermined admixture of (a) a methylol compound, or its equivalent, and (b) an iodopropynyl compound:

- (1) Iodopropynyl compounds are substantially water insoluble at weight ratios of (a):(b) of less than 100; accordingly, at weight ratios below 100:1, it is difficult to uniformly distribute the iodopropynyl compound in aqueous use compositions, particularly in creams, gels and the like. In this invention, the admixtures are used at a weight ratio of (a):(b) of 100:1 to 2000:1, which are water soluble in all use compositions at conventional use levels.
- (2) Effective synergistic biocidal activity is achieved for admixtures having a weight ratio of (a):(b) of 100:1 to 2000:1. Such admixtures have a Synergistic Index (SI) value approaching zero (maximum synergism) for a wide range of organisms. In contrast, admixtures with (a):(b) ratios below 100:1, e.g. 10:1 to 50:1, are much less synergistic, and are active with only a narrower range of organisms.
- (3) Preservative activity for use compositions is achieved most effectively with an admixture wt. ratio of 100:1 to 2000:1 at use levels of 0.05 to 2% by weight of the finished product. In this amount, the iodopropynyl compound is present in an amount of only 0.5-10 ppm, which significantly reduces the cost and toxicity of the use composition. The methylol compound also is present in an amount of at least 250 ppm.

The experimental results upon which these discoveries are based are described below. In these examples, the (a) methylol compound may be selected from diazolidinyl urea (GERMALL® II) N-[1,3-bis(hydroxymethyl)-2,5-dioxo-4-imidazolidinyl]-N,N'-bis(hydroxymethyl) urea, imidurea (GERMALL® 115),

1,3-dimethylol-5,5-dimethyl hydantoin (DMDMH), sodium hydroxymethylglycinate (SUTTOCIDE® A), glycine anhydride dimethylol (GADM), dimethylhydroxymethyl pyrazole, (1-(3-chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride (a methylol equivalent), 1,3,5-(trishydroxy-ethyl)hexahydrotriazine, or hydroxymethyl pyrrolidone; and the (b) iodopropynyl compound is iodopropynyl alcohol (IPGA) or 3-iodo-2-propynylbutyl carbamate (IPBC).

1. WATER SOLUBILITY

The water solubility or insolubility of admixtures of several methylol compounds with IPBC as 1% aqueous solutions is shown in Tables A through C below.

TABLE A						
Weight Ratio of Germall® II:IPBC	Amount in ppm	Solubility				
2000:1	5	Soluble				
1000:1	10	Soluble				
500:1	20	Soluble				
200:1	50	Soluble				
100:1	100	Soluble				
50:1	200	Insoluble				
20:1	500	Insoluble				
	TABLE B					
Weight Ratio of GADM: IPBC	Amount in ppm	Solubility				
2000:1	5	Soluble				
1000:1	10	Soluble				
500:1	20	Soluble				
200:1	50	Soluble				
100:1	100	Soluble				
50:1	200	Insoluble				
20:1	500	Insoluble				

TABLE C

Weight Ratio of DMDMH:IPBC	Amount in ppm	Solubility
2000:1	5	Soluble
1000:1	10	Soluble
500:1	20	Soluble
200:1	50	Soluble
100:1	100	Soluble
50:1	200	Insoluble
20:1	500	Insoluble

These results demonstrate that admixtures having a ratio of 50:1 or 20:1 are insoluble in water whereas at ratios of 100:1 to 2000:1 the admixtures are soluble in water.

2. SYNERGISM

Tables 1 through 14 below demonstrate the very effective synergistic interaction between compounds "a" and "b" against a broad range of fungi and both gramnegative and gram-positive bacteria. The following organisms were tested:

-	-	_	_
n	,,,,		•

Organism	Number	Inoculum Concentration
Ps. aeruginosa (PSA)*	9027	2.1×10^6 CFU/gm of Product
E. coli (ECOLI)*	8739	4.7×10^5 CFU/gm of Product
Staph. aureus (SA) **	6538	1.6 \times 10 ⁶ CFU/gm of Product
Ps. cepacia (PC)*	25416	1.6 \times 10 ⁶ CFU/gm of Product
C. albicans (CAN) ***	10231	8.0×10^4 CFU/gm of Product
A. niger (AN)***	16404	2.7×10^5 CFU/gm of Product

Table D below lists the static (MIC) and cidal activities of several antimicrobial agents in ppm. These activities are used to calculate the Synergism Index (SI) of admixtures of the present invention.

^{*} gram-negative bacteria

^{**} gram-positive bacteria

^{***} fungi

TABLE D

Static (MIC) and Cidal Activities of Several Antimicrobial Compounds

(mdd ui	
<u>Concentrations</u>	
(Static/Cidal	

Organism					
(ATCC #)	IPBC	Germall@ II	GADM	DMDMH	IPGA
(SA) (6538)	100/200	400/1600	400/800	450/1600	300/2000
(ECOLI) (8739)	50/100	400/1600	400/800	400/800	150/600
(PSA) (9027)	800/1200	400/1600	400/400	000/1600	01/01
(PC) (25416)	1200/1800	200/400	200/400	000/1600	70/300
(CAN) (10231)	50/100	1500/15000	7500/15000	8000/16000	50/300
(AN) (16404)	50/100	3200/3200	1600/3200	8000/16000	30/30

The Synergism Index was determined by the same mathematical treatment of such data described by Kull et al. in Applied Microbiology 9,538-541 (1961) using the following relationship:

Synergism Index (SI) =
$$Q_A$$
 + Q_B Q_b

where:

- 1. Q_a = The quantity of Compound a acting alone, producing an endpoint.
- 2. $Q_b =$ The quantity of Compound b acting alone, producing and endpoint.
- 3. Q_A = The quantity of Compound \underline{A} in mixture, producing an endpoint.
- 4. $Q_B =$ The quantity of Compound \underline{B} in mixture, producing an endpoint.

When SI is equal to 1, a mere additive effect of the components in the mixture is indicated; when SI is less than 1, synergism has occurred; and when SI is greater than 1 it indicates antagonism of the two components.

According to this well known method of measuring synergism, the quantity of each component in the various mixtures is compared with the quantity of pure component that is required to reach the same endpoint or to produce the same microbiological effect as the mixture.

TABLE 1
2000:1 Wt. Ratio GERMALL® II/IPBC

Use Level	Organism	O _a _	<u> </u>	Q _A	O _B	sı
0.01%	SA	200	1600	0.05	99.95	0.06
H .	ECOLI	100	1600	0.05	99.95	0.06
ti	PSA	1200	1600	0.05	99.95	0.06
11	PC	1800	1250	0.05	99.95	0.08
11	CAN	100	15000	0.05	99.95	0.01
H .	AN	100	3200	0.05	99.95	0.03
<u>Use Level</u>	Organism	O_a_	O _b	O _A _	O _B	SI
0.025%	SA	200	1600	0.125	249.9	0.16
**	ECOLI	100	1600	0.125	249.9	0.16
ŧī	PSA	1200	1600	0.125	249.9	0.16
11	PC	1800	1250	0.125	249.9	0.20
FF	CAN	100	15000	0.125	249.9	0.02
**	AN	100	3200	0.125	249.9	0.08
<u>Use Level</u>	Organism	O _a _	O _b	O _A	O _B	SI
0.05%	SA	200	1600	0.25	499.8	0.31
11	ECOLI	100	1600	0.25	499.8	0.31
***	PSA	1200	1600	0.25	499.8	0.31
11	PC	1800	1250	0.25	499.8	0.40
11	CAN	100	15000	0.25	499.8	0.04
11	AN	100	3200	0.25	499.8	0.16
<u>Use Level</u>	Organism	O _a _	O _b	O _A	O _B	si
0.10%	SA	200	1600	0.5	999.5	0.63
11	ECOLI	100	1600	0.5	999.5	0.63
Ħ	PSA	1200	1600	0.5	999.5	0.63
*1	PC	1800	1250	0.5	999.5	0.80
ŧŧ	CAN	100	15000	0.5	999.5	0.07
**	AN	100	3200	0.5	999.5	0.32

TABLE 1 (CONT)

<u>Use Level</u>	Organism	O _a .	<u> </u>	O _A	Q _B	SI
0.20%	SA	200	1600	1	1999	1.25
11	ECOLI	100	1600	1	1999	1.26
11	PSA	1200	1600	1	1999	1.25
11	PC	1800	1250	1	1999	1.60
ti	CAN	100	15000	1	1999	0.14
ti	AN	100	3200	1	1999	0.63

<u>Use Level</u>	Organism	Q _a .	Q _b	Q _A	Q _B	SI
0.40%	SA	200	1600	2	3998	2.51
11	ECOLI	100	1600	2	3998	2.52
**	PSA	1200	1600	2	3998	2.50
81	PC	1800	1250	2	3998	3.20
61	CAN	100	15000	2	3998	0.29
11	AN	100	3200	2	3998	1.27

<u>Use Level</u>	<u>Organism</u>	O _a .	Q _b	Q_{Λ}	O _R	SI	_
0.50%	SA	200	1600	2.5	4997.5	3.14	
29	ECOLI	100	1600	2.5	4997.5	3.15	
**	PSA	1200	1600	2.5	4997.5	3.13	
41	PC	1800	1250	2.5	4997.5	4.00	
10	CAN	100	15000	2.5	4997.5	0.36	
11	AN	100	3200	2.5	4997.5	1.59	

TABLE 2

1000:1 Wt. Ratio GERMALL® II/IPBC

Use Level	Organism	O _a	Q _b	<u>Q</u> _A	Q _R	SI
0.01%	SA	200	1600	0.1	99.9	0.06
**	ECOLI	100	1600	0.1	99.9	0.06
**	PSA	1200	1600	0.1	99.9	0.06
11	PC	1800	1250	0.1	99.9	0.08
ŧı	CAN	100	15000	0.1	99.9	0.01
Ħ	AN	100	3200	0.1	99.9	0.03
<u>Use Level</u>	Organism	Q _a _	Q _b	Q _A _	O _B _	SI
0.025%	SA	200	1600	0.25	249.8	0.16
ti	ECOLI	100	1600	0.25	249.8	0.16
11	PSA	1200	1600	0.25	249.8	0.16
11	PC	1800	1250	0.25	249.8	0.20
11	CAN	100	15000	0.25	249.8	0.02
**	AN	100	3200	0.25	249.8	0.08
	Organism	O _a _	O _b	O _A	O _B	sı
0.05%	SA	200	1600	0.5	499.5	0.31
11	ECOLI	100	1600	0.5	499.5	0.32
11	PSA	1200	1600	0.5	499.5	0.31
**	PC	1800	1250	0.5	499.5	0.40
11	CAN	100	15000	0.5	499.5	0.04
**	AN	100	3200	0.5	499.5	0.16
Use Level	Organism	Q _a _	o _b	O _A	O _B	SI
0.10%	SA	200	1600	1	999	0.63
	ECOLI	100	1600	1	999	0.63
***	PSA	1200	1600	1	999	0.63
**	PC	1800	1250	1	999	0.80
61	CAN	100	15000	1	999	0.08
Ħ	AN	100	3200	1	999	0.32

TABLE 2 (CONT)

Use Level	Organism	Q _a	Q _b	O _A _	O _B	SI
0.20%	SA	200	1600	2	1998	1.26
11	ECOLI	100	1600	2	1998	1.27
11	PSA	1200	1600	2	1998	1.25
**	PC	1800	1250	2	1998	1.60
11	CAN	100	15000	2	1998	0.15
11	AN	100	3200	2	1998	0.64
<u>Use Level</u>	Organism	Q_a	Q _b	Q _A	Q _B	SI
0.40%	SA	200	1600	4	3996	2.52
89	ECOLI	100	1600	4	3996	2.54
91	PSA	1200	1600	4	3996	2.50
11	PC	1800	1250	4	3996	3.20
II	CAN	100	15000	4	3996	0.31
11	AN	100	3200	4	3996	1.29
<u>Use Level</u>	Organism	O _a .	O _b	O _A	O _B	SI_
0.50%	SA	200	1600	5	4995	3.15
ti	ECOLI	100	1600	5	4995	3.17
11	PSA	1200	1600	5	4995	3.13
II	PC	1800	1250	5	4995	4.00
17	CAN	100	15000	5	4995	0.38
11	AN	100	3200	5	4995	1.61

TABLE 10
500:1 Wt. Ratio GERMALL® II/IPBC

Use Level	Organism	<u>Q</u> a_	<u> </u>	Q _A	O _B	SI
0.01%	SA	200	1600	0.2	99.8	0.06
11	ECOLI	100	1600	0.2	99.8	0.06
41	PSA	1200	1600	0.2	99.8	0.06
11	PC	1800	1250	0.2	99.8	0.08
ti	CAN	100	15000	0.2	99.8	0.01
tī	AN	100	3200	0.2	99.8	0.03
Use Level	Organism	O _a	Q _b	O _A	O _B	SI
0.025%	SA	200	1600	0.5	249.5	0.16
**	ECOLI	100	1600	0.5	249.5	0.16
11	PSA	1200	1600	0.5	249.5	0.16
11	PC	1800	1250	0.5	249.5	0.20
*1	CAN	100	15000	0.5	249.5	0.02
11	AN	100	3200	0.5	249.5	0.08
<u>Use Level</u>	Organism	O _a .	O _b	O _A	O_B	SI
0.05%	SA	200	1600	1	499	0.32
**	ECOLI	100	1600	1	499	0.32
e 1	PSA	1200	1600	1	499	0.31
**	PC	1800	1250	1	499	0.40
**	CAN	100	15000	1	499	0.04
**	AN	100	3200	1	499	0.17
<u>Use Leve</u>	Organism	O _a .	O _b	O _A	O _B	SI
0.10%	SA	200	1600	2	998	0.63
tt	ECOLI	100	1600	2	998	0.64
11	PSA	1200	1600	2	998	0.63
17	PC	1800	1250	2	998	0.80
H	CAN	100	15000	2	998	0.09
* f	AN	100	3200	2	998	0.33

TABLE 3 (CONT)

<u>Use Level</u>	Organism	O _a .	O _b	O _A _	O _B	sı
0.20%	SA	200	1600	4	1996	1.27
er	ECOLI	100	1600	4	1996	1.29
11	PSA	1200	1600	4	1996	1.25
11	PC	1800	1250	4	1996	1.60
It	CAN	100	15000	4	1996	0.17
tt	AN	100	3200	4	1996	0.66
Use Level	Organism	<u>Q</u> a_	Q _b	O _A	Q _R	sı
0.40%	SA	200	1600	8	3992	2.54
11	ECOLI	100	1600	8	3992	2.58
11	PSA	1200	1600	8	3992	2.50
t1	PC	1800	1250	8	3992	3.20
11	CAN	100	15000	8	3992	0.35
11	AN	100	3200	8	3992	1.33
<u>Use Level</u>	Organism	Q _a _	O _b	O _A	O _B	sı
0.50%	SA	200	1600	10	4990	3.17
**	ECOLI	100	1600	10	4990	3.22
11	PSA	1200	1600	10	4990	3.13
11	PC	1800	1250	10	4990	4.00
11	CAN	100	15000	10	4990	0.43
11	AN	100	3200	10	4990	1.66

TABLE 4
200:1 Wt. Ratio GERMALL® II/IPBC

<u>Use</u> Level	Organism	Q _a	<u>Q</u> b	O _A	O _R	SI	
0.01%	SA	200	1600	0.5	99.5	0.06	
11	ECOLI	100	1600	0.5	99.5	0.07	
**	PSA	1200	1600	0.5	99.5	0.06	
11	PC	1800	1250	0.5	99.5	0.08	
**	CAN	100	15000	0.5	99.5	0.01	
11	AN	100	3200	0.5	99.5	0.04	
<u>Use Level</u>	Organism	O _a .	O _b	O _A _	O _B	SI	
0.025%	SA	200	1600	1.25	248.75	0.16	
**	ECOLI	100	1600	1.25	248.75	0.17	
11	PSA	1200	1600	1.25	248.75	0.16	
**	PC	1800	1250	1.25	248.75	0.20	
**	CAN	100	15000	1.25	248.75	0.03	
11	AN	100	3200	1.25	248.75	0.09	
<u>Use Level</u>	Organism	O _a	O _b	Q _A	O _B	SI	
0.05%	SA	200	1600	2.5	497.5	0.32	
ŧī	ECOLI	100	1600	2.5	497.5	0.34	
17	PSA	1200	1600	2.5	497.5	0.31	
91	PC	1800	1250	2.5	497.5	0.40	
†1	CAN	100	15000	2.5	497.5	0.06	
**	AN	100	3200	2.5	497.5	0.18	
<u>Use Level</u>	Organism	O _a _	O _b	O _A	O_B	SI	
0.10%	SA	200	1600	5	995	0.65	
11	ECOLI	100	1600	5	995	0.67	
11	PSA	1200	1600	5	995	0.63	
11	PC	1800	1250	5	995	0.80	
II .	CAN	100	15000	5	995	0.12	
tt	AN	100	3200	5	995	0.36	

TABLE 4 (CONT)

Use Level	Organism	Q _a	Q _b	O _A	O _B	SI
0.20%	SA	200	1600	10	1990	1.29
11	ECOLI	100	1600	10	1990	1.34
11	PSA	1200	1600	10	1990	1.25
11	PC	1800	1250	10	1990	1.60
89	CAN	100	15000	10	1990	0.23
11	AN	100	3200	10	1990	0.72

Use Level	Organism	Q _a _	O _b	Q _A	O _B	SI
0.40%	SA	200	1600	20	3980	2.59
11	ECOLI	100	1600	20	3980	2.69
11	PSA	1200	1600	20	3980	2.50
ti	PC	1800	1250	20	3980	3.20
11	CAN	100	15000	20	3980	0.47
tt	AN	100	3200	20	3980	1.44

Use Level	Organism	Q _a _	O _b	O _A	Q _B	SI	-
0.50%	SA	200	1600	25	4975	3.23	
11	ECOLI	100	1600	25	4975	3.36	
11	PSA	1200	1600	25	4975	3.13	
11	PC	1800	1250	25	4975	3.99	
tt	CAN	100	15000	25	4975	0.58	
BT .	AN	100	3200	25	4975	1.80	

- 17 -

TABLE 5

100:1 Wt. Ratio GERMALL® II/IPBC

<u>Use Level</u>	Organism	O _a .	Q _b	O _A	O _B	SI
0.01%	SA	200	1600	1	99	0.07
11	ECOLI	100	1600	1	99	0.07
77	PSA	1200	1600	1	99	0.06
61	PC	1800	1250	1	99	0.08
Ħ	CAN	100	15000	1	99	0.02
#1	AN	100	3200	1	99	0.04
<u>Use Level</u>	Organism	Q _a	Q _b	O _A	Q _B	SI
0.025%	SA	200	1600	2.5	248	0.17
91	ECOLI	100	1600	2.5	248	0.18
11	PSA	1200	1600	2.5	248	0.16
11	PC	1800	1250	2.5	248	0.20
97	CAN	100	15000	2.5	248	0.04
11	AN	100	3200	2.5	248	0.10
<u>Use Level</u>	Organism	<u>Q</u> a	O _b	Q _A	O_B	sī
0.05%	SA	200	1600	5	495	0.33
*1	ECOLI	100	1600	5	495	0.36
*1	PSA	1200	1600	5	495	0.31
11	PC	1800	1250	5	495	0.40
88	CAN	100	15000	5	495	0.08
79	ИA	100	3200	5	495	0.20
<u>Use Level</u>	<u>Organism</u>	Q _a .	O _b	O _A	O _B	si
0.10%	SA	200	1600	10	990	0.67
11	ECOLI	100	1600	10	990	0.72
**	PSA	1200	1600	10	990	0.63
**	PC	1800	1250	10	990	0.80
**	CAN	100	15000	10	990	0.17
11	AN	100	3200	10	990	0.41

TABLE 5 (CONT)

<u>Use Level</u>	Organism	Q _a	O _b	O _A	O_B	SI	
0.20%	SA	200	1600	20	1980	1.34	
11	ECOLI	100	1600	20	1980	1.44	
11	PSA	1200	1600	20	1980	1.25	
11	PC	1800	1250	20	1980	1.60	
11	CAN	100	15000	20	1980	0.33	
11	AN	100	3200	20	1980	0.82	

<u>Use Level</u>	Organism	Q _a _	Q _b	Q _A	O _B	_sı
0.40%	SA	200	1600	40	3960	2.68
61	ECOLI	100	1600	40	3960	2.88
11	PSA	1200	1600	40	3960	2.51
*1	PC	1800	1250	40	3960	3.19
11	CAN	100	15000	40	3960	0.66
11	AN	100	3200	40	3960	1.64

<u>Use</u> Level	Organism	Q _a _	O _b	Q _A	O _B	SI
0.50%	SA	200	1600	50	4950	3.34
#1	ECOLI	100	1600	50	4950	3.59
11	PSA	1200	1600	50	4950	3.14
**	PC	1800	1250	50	4950	3.99
11	CAN	100	15000	50	4950	0.83
11	AN	100	3200	50	4950	2.05

TABLE 6
50:1 Wt. Ratio GERMALL® II/IPBC

<u>Use Level</u>	Organism	O _a .	Q _b	O _A	Q _B	SI
0.01%	SA	200	1600	2	98	0.07
11	ECOLI	100	1600	2	98	0.08
11	PSA	1200	1600	2	98	0.06
11	PC	1800	1250	2	98	0.08
91	CAN	100	15000	2	98	0.03
65	AN	100	3200	2	98	0.05
<u>Use Level</u>	Organism	Q _a	o b	Q _A	O _B	SI
0.025%	SA	200	1600	5	245	0.18
11	ECOLI	100	1600	5	245	0.20
tr	PSA	1200	1600	5	245	0.16
11	PC	1800	1250	5	245	0.20
ti	CAN	100	15000	5	245	0.07
11	AN	100	3200	5	245	0.13
	Organism	O _a _	O _b	O _A	O_B	SI
0.05%	SA	200	1600	10	490	0.36
11	ECOLI	100	1600	10	490	0.41
11	PSA	1200	1600	10	490	0.31
11	PC	1800	1250	10	490	0.40
ti	CAN	100	15000	10	490	0.13
11	AN	100	3200	10	490	0.25
	_					
	Organism	Q _a _	<u>Q</u> b	O _A	Q _B	SI
0.10%	SA	200	1600	20	980	0.71
81	ECOLI	100	1600	20	980	0.81
11	PSA	1200	1600	20	980	0.63
Ħ	PC	1800	1250	20	980	0.80
e1	CAN	100	15000	20	980	0.27
11	AN	100	3200	20	980	0.51

TABLE 6 (CONT)

Use Level	Organism	O _a	O _b	Q _A _	O _B	SI
0.20%	SA	200	1600	40	1960	1.43
11	ECOLI	100	1600	40	1960	1.63
pr .	PSA	1200	1600	40	1960	1.26
¢1	PC	1800	1250	40	1960	1.59
•	CAN	100	15000	40	1960	0.53
11	AN	100	3200	40	1960	1.01

Use Level	Organism	Q _a	Q _b	Q _A	O _B	SI
0.40%	SA	200	1600	80	3920	2.85
11	ECOLI	100	1600	80	3920	3.25
Ħ	PSA	1200	1600	80	3920	2.52
ŧī	PC	1800	1250	80	3920	3.18
†1	CAN	100	15000	80	3920	1.06
ŧī	AN	100	3200	80	3920	2.03

Use Level	Organism	Q_	Q _h	<u>Q</u> 2	Q _B	SI
0.50%	SA	200	1600	100	4900	3.56
11	ECOLI	100	1600	100	4900	4.06
**	PSA	1200	1600	100	4900	3.15
11	PC	1800	1250	100	4990	3.98
11	CAN	100	15000	100	4900	1.33
91	AN	100	3200	100	4900	2.53

TABLE 7
20:1 Wt. Ratio GERMALL® II/IPBC

Use Level	Organism	Q _a _	O _b	O _A	O _B	SI
0.01%	SA	200	1600	5	95	0.08
**	ECOLI	100	1600	5	95	0.11
11	PSA	1200	1600	5	95	0.06
11	PC	1800	1250	5	95	0.08
11	CAN	100	15000	5	95	0.06
11	MA	100	3200	5	95	0.08
<u>Use Level</u>	Organism	Q _a	O _b	O _A	O _B	SI
0.025%	SA	200	1600	12.5	237.5	0.21
**	ECOLI	100	1600	12.5	237.5	0.27
11	PSA	1200	1600	12.5	237.5	0.16
11	PC	1800	1250	12.5	237.5	0.20
17	CAN	100	15000	12.5	237.5	0.14
11	AN	100	3200	12.5	237.5	0.20
<u>Use Level</u>	Organism	Q _a .		Q _A	O _B	SI
0.05%	SA	200	1600	25	475	0.42
11	ECOLI	100	1600	25	475	0.55
11	PSA	1200	1600	25	475	0.32
11	PC	1800	1250	25	475	0.39
er	CAN	100	15000	25	475	0.28
11	AN	100	3200	25	475	0.40
<u>Use Level</u>	Organism	Q _a .	<u>o</u> b	O _A	O _B	SI
0.10%	SA	200	1600	50	950	0.84
11	ECOLI	100	1600	50	950	1.09
11	PSA	1200	1600	50	950	0.64
11	PC	1800	1250	50	950	0.79
11	CAN	100	15000	50	950	0.56
11		100				0.80

TABLE 7 (CONT)

Use Level	Organism_	Q _a	<u> </u>	Q _A	O _B	SI
0.20%	SA	200	1600	100	1900	1.69
**	ECOLI	100	1600	100	1900	2.19
11	PSA	1200	1600	100	1900	1.27
**	PC	1800	1250	100	1900	1.58
81	CAN	100	15000	100	1900	1.13
11	AN	100	3200	100	1900	1.59
<u>Use Level</u>	Organism	O _a _	o _b	O _A	Q _B	si
0.40%	SA	200	1600	200	4800	4.00
11	ECOLI	100	1600	200	4800	5.00
11	PSA	1200	1600	200	4800	3.17
er	PC	1800	1250	200	4800	3.95
ŧı	CAN	100	15000	200	4800	2.32
17	AN	100	3200	200	4800	3.50
<u>Use Level</u>	Organism	Q _a .	Q _b	Q _A	Q _B	sı
0.50%	SA	200	1600	250	4750	4.22
11	ECOLI	100	1600	250	4750	5.47
**	PSA	1200	1600	250	4750	3.18
11	PC	1800	1250	250	4750	3.94
**	CAN	100	15000	250	4750	2.82
**	AN	100	3200	250	4750	3.98

TABLE 8
2000:1 Wt. Ratio DMDMH/IPBC

Use Level	Organism	O _a	O _b	_Q _A	O _B	SI
0.01%	SA	200	1600	0.05	99.95	0.06
11	ECOLI	100	800	0.05	99.95	0.13
ŧŧ	PSA	1200	1600	0.05	99.95	0.06
ti	PC	1800	1600	0.05	99.95	0.06
Ħ	CAN	100	16000	0.05	99.95	0.01
91	AN	100	16000	0.05	99.95	0.01

Use Level	Organism	Q _a	<u>Q</u> b	<u>Q</u>	Q _B	SI
0.025%	SA	200	1600	0.125	249.88	0.16
91	ECOLI	100	800	0.125	249.88	0.31
***	PSA	1200	1600	0.125	249.88	0.16
H	PC	1800	1600	0.125	249.88	0.16
11	CAN	100	16000	0.125	249.88	0.02
11	AN	100	16000	0.125	249.88	0.02

Use Level	Organism	Q _a _	Q _b	O _A	O _B	SI
0.05%	SA	200	1600	0.25	499.75	0.31
11	ECOLI	100	800	0.25	499.75	0.63
11	PSA	1200	1600	0.25	499.75	0.31
11	PC	1800	1600	0.25	499.75	0.31
81	CAN	100	16000	0.25	499.75	0.03
17	AN	100	16000	0.25	499.75	0.03

Use Level	Organism	O _a	<u> </u>	O _A	O _B	<u>SI</u>
0.10%	SA	200	1600	0.5	999.5	0.63
\$1	ECOLI	100	800	0.5	999.5	1.25
et	PSA	1200	1600	0.5	999.5	0.63
11	PC	1800	1600	0.5	999.5	0.62
11	CAN	100	16000	0.5	999.5	0.07
11	AN	100	16000	0.5	999.5	0.07

TABLE 8 (CONT)

<u>Use Level</u>	Organism	O_a	O _b	O _A	O_B	SI
0.20%	SA	200	1600	1	1999	1.25
11	ECOLI	100	800	1	1999	2.51
11	PSA	1200	1600	1	1999	1.25
71	PC	1800	1600	. 1	1999	1.25
11	CAN	100	16000	1	1999	0.13
11	AN	100	16000	1	1999	0.13
Use Level	Organism	O _a	O _b	O _A	O _B	sı
0.40%	SA	200	1600	2	3998	2.51
**	ECOLI	100	800	2	3998	5.02
11	PSA	1200	1600	2	3998	2.50
*11	PC	1800	1600	2	3998	2.50
**	CAN	100	16000	2	3998	0.27
11	AN	100	16000	2	3998	0.27
<u>Use Level</u>	Organism	O _a	O _b	O _A	O _B	SI
0.50%	SA	200	1600	2.5	4997.5	3.14
11	ECOLI	100	800	2.5	4997.5	6.27
**	PSA	1200	1600	2.5	4997.5	3.13
**	PC	1800	1600	2.5	4997.5	3.12
11	CAN	100	16000	2.5	4997.5	0.34
*1	AN	100	16000	2.5	4997.5	0.34
				•		

TABLE 9
1000:1 Wt. Ratio DMDMH/IPBC

Use Level	Organism	Q _a	O _b	Q _A	O _B	SI
0.01%	SA	200	1600	0.1	99.9	0.06
11	ECOLI	100	800	0.1	99.9	0.13
1 7	PSA	1200	1600	0.1	99.9	0.06
11	PC	1800	1600	0.1	99.9	0.06
#1	CAN	100	16000	0.1	99.9	0.01
tt	AN	100	16000	0.1	99.9	0.01
Use Level	Organism	O _a	O _b	O _A	Q _B	sı
0.025%	SA	200	1600	0.25	249.8	0.16
11	ECOLI	100	800	0.25	249.8	0.31
91	PSA	1200	1600	0.25	249.8	0.16
ti	PC	1800	1600	0.25	249.8	0.16
li .	CAN	100	16000	0.25	249.8	0.02
tr	AN	100	16000	0.25	249.8	0.02
<u>Use Level</u>	Organism	Q	O _b	Q _A	O _B	SI
0.05%	SA	200	1600	0.5	499.5	0.31
11	ECOLI	100	800	0.5	499.5	0.63
11	PSA	1200	1600	0.5	499.5	0.31
11	PC	1800	1600	0.5	499.5	0.31
17	CAN	100	16000	0.5	499.5	0.04
IT	AN	100	16000	0.5	499.5	0.04
Use Level	Organism	Q _a	O _b	_O _A	O_B	SI
0.10%	SA	200	1600	1	999	0.63
31	ECOLI	100	800	1	999	1.26
11	PSA	1200	1600	1	999	0.63
91	PC	1800	1600	1	999	0.62
11	CAN	100	16000	1	999	0.07
EI .	AN	100	16000	1	999	0.07

TABLE 9 (CONT)

Use Level	Organis	n O	2 _a	O _A	O _B	SI
0.20%	SA	20	0 1600	2	1998	1.26
11	ECOLI	10	008 00	2	1998	2.52
11	PSA	120	0 1600	2	1998	1.25
11	PC	180	0 1600	2	1998	1.25
11	CAN	10	0 16000	2	1998	0.14
11	AN	10	0 16000	2	1998	0.14
<u>Use Level</u>	Organism	O	Q _b	Q _A	O _B	si
0.40%	SA	200	1600	4	3996	2.52
eT	ECOLI	100	800	4	3996	5.04
11	PSA	1200	1600	4	3996	2.50
11	PC	1800	1600	4	3996	2.50
••	CAN	100	16000	4	3996	0.29
91	AN	100	16000	4	3996	0.29
<u>Use Level</u>	Organism	Q _a _	Q _b	O _A	O _B	SI
0.50%	SA	200	1600	5	4995	3.15
F1	ECOLI	100	800	5	4995	6.29
II	PSA	1200	1600	5	4995	3.13
11	PC	1800	1600	5	4995	3.12
11	CAN	100	16000	5	4995	0.36

AN 100 16000 2.5 4997.5 0.36

- 27 -

TABLE 10
500:1 Wt. Ratio DMDMH/IPBC

Use Level	Organism	O _a _	o _b	O _A	O	SI
0.01%	SA	200	1600	0.2	99.8	0.06
91	ECOLI	100	800	0.2	99.8	0.13
88	PSA	1200	1600	0.2	99.8	0.06
Ħ	PC	1800	1600	0.2	99.8	0.06
••	CAN	100	16000	0.2	99.8	0.01
*1	AN	100	16000	0.2	99.8	0.01
Use Level	Organism	Q _a	O _b	O _A	O _B	SI
0.25%	SA	200	1600	0.5	249.5	0.16
11	ECOLI	100	800	0.5	249.5	0.32
11	PSA	1200	1600	0.5	249.5	0.16
11	PC	1800	1600	0.5	249.5	0.16
11	CAN	100	16000	0.5	249.5	0.02
tt	AN	100	16000	0.5	249.5	0.02
Use Level	Organism	O,	O _b		O _A O	sı
0.05%	SA	200	1600		499	0.32
**	ECOLI	100	800) 1	499	0.63
11	PSA	1200	1600) 1	499	0.31
81	PC	1800	1600) 1	499	0.31
11	CAN	100	16000) 1	499	0.04
**	AN	100	16000) 1	499	0.04
Use Level	Organism	Q _a _	O _b	O,	O _B	SI
0.10%	SA	200	1600	•	998	0.63
11	ECOLI	100	800	2	998	1.27
81	PSA	1200	1600		998	0.63

1800 1600

16000

16000

100

100

2

2

2

998

998

998

0.62

0.08

0.08

PC

AN

CAN

TABLE 10 (CONT)

Use Level	Organism	<u>Q</u> a_	Q _b	Q _A	O_B	<u>sı</u>
0.20%	SA	200	1600	4	1996	1.27
11	ECOLI	100	800	4	1996	2.54
11	PSA	1200	1600	4	1996	1.25
*1	PC	1800	1600	4	1996	1.25
11	CAN	100	16000	4	1996	0.16
91	AN	100	16000	4	1996	0.16

Use <u>Leve</u>	1 Organism	Q _a	O _b	Q _A	Q _B	SI
0.40%	SA	200	1600	8	3992	2.54
n	ECOLI	100	800	8	3992	5.07
17	PSA	1200	1600	8	3992	2.50
51	PC	1800	1600	8	3992	2.50
11	CAN	100	16000	8	3992	0.33
**	AN	100	16000	8	3992	0.33

Use Level	Organism	Q _a _	O _b	Q _A	O _B	SI
0.50%	SA	200	1600	10	4900	3.11
**	ECOLI	100	800	10	4900	6.23
61	PSA	1200	1600	10	4900	3.07
TI .	PC	1800	1600	10	4900	3.07
17	CAN	100	16000	10	4900	0.41
tt	AN	100	16000	10	4900	0.41

TABLE 11
200:1 Wt. Ratio DMDMH/IPBC

Use Level	Organism	O _a _	Q _b	O _A	Q _B	si
0.01%	SA	200	1600	0.5	99.5	0.06
11	ECOLI	100	800	0.5	99.5	0.13
11	PSA	1200	1600	0.5	99.5	0.06
61	PC	1800	1600	0.5	99.5	0.06
11	CAN	100	16000	0.5	99.5	0.01
11	AN	100	16000	0.5	99.5	0.01
<u>Use Level</u>	Organism	<u>Q</u> a	O _b	Q _A _	O _B	SI
0.025%	SA	200	1600	1.25	248.75	0.16
11	ECOLI	100	800	1.25	248.75	0.32
11	PSA	1200	1600	1.25	248.75	0.16
**	PC	1800	1600	1.25	248.75	0.16
11	CAN	100	16000	1.25	248.75	0.03
FT	AN	100	16000	1.25	248.75	0.03
<u>Use Level</u>	Organism	Q _a _	Q _b	O _A	Q _B	SI
Use Level	Organism SA		Q _b	O _A	O _B	SI 0.32
			_	••	_	
0.05%	SA	200	1600	2.5	497.5	0.32
0.05%	SA ECOLI	200 100	1600 800	2.5 2.5	497.5 497.5	0.32 0.65
0.05%	SA ECOLI PSA	200 100 1200	1600 800 1600	2.5 2.5 2.5	497.5 497.5 497.5	0.32 0.65 0.31
0.05%	SA ECOLI PSA PC	200 100 1200 1800	1600 800 1600	2.5 2.5 2.5 2.5	497.5 497.5 497.5 497.5	0.32 0.65 0.31 0.31
0.05% " " " "	SA ECOLI PSA PC CAN	200 100 1200 1800 100	1600 800 1600 1600	2.5 2.5 2.5 2.5 2.5	497.5 497.5 497.5 497.5 497.5	0.32 0.65 0.31 0.31 0.06
0.05% " " " "	SA ECOLI PSA PC CAN	200 100 1200 1800 100	1600 800 1600 1600	2.5 2.5 2.5 2.5 2.5	497.5 497.5 497.5 497.5 497.5	0.32 0.65 0.31 0.31 0.06
0.05% "" "" "" ""	SA ECOLI PSA PC CAN AN	200 100 1200 1800 100	1600 800 1600 1600 16000	2.5 2.5 2.5 2.5 2.5 2.5	497.5 497.5 497.5 497.5 497.5 497.5	0.32 0.65 0.31 0.31 0.06 0.06
0.05% " " " " " " "	SA ECOLI PSA PC CAN AN Organism	200 100 1200 1800 100 100	1600 800 1600 1600 16000	2.5 2.5 2.5 2.5 2.5 2.5 2.5	497.5 497.5 497.5 497.5 497.5 497.5	0.32 0.65 0.31 0.31 0.06 0.06
0.05% " " " " " " Use Level 0.10%	SA ECOLI PSA PC CAN AN Organism SA	200 100 1200 1800 100 100	1600 800 1600 16000 16000	2.5 2.5 2.5 2.5 2.5 2.5 2.5	497.5 497.5 497.5 497.5 497.5 497.5	0.32 0.65 0.31 0.31 0.06 0.06
0.05% " " " " " " " Use Level 0.10% "	SA ECOLI PSA PC CAN AN Organism SA ECOLI	200 100 1200 1800 100 100	1600 800 1600 16000 16000 0 0 16000 800	2.5 2.5 2.5 2.5 2.5 2.5 2.5 5	497.5 497.5 497.5 497.5 497.5 497.5 995	0.32 0.65 0.31 0.31 0.06 0.06
0.05% " " " " " " " " Use Level 0.10% "	SA ECOLI PSA PC CAN AN Organism SA ECOLI PSA	200 100 1200 1800 100 100 200 100 1200	1600 800 1600 16000 16000 16000 800 1600	2.5 2.5 2.5 2.5 2.5 2.5 5 5	497.5 497.5 497.5 497.5 497.5 497.5 995 995	0.32 0.65 0.31 0.31 0.06 0.06 SI 0.65 1.29 0.63
0.05% " " " " Use Level 0.10% " "	SA ECOLI PSA PC CAN AN Organism SA ECOLI PSA PC	200 100 1200 1800 100 200 100 1200 1800	1600 800 1600 16000 16000 0 _b 1600 800 1600	2.5 2.5 2.5 2.5 2.5 2.5 5 5	497.5 497.5 497.5 497.5 497.5 497.5 995 995 995	0.32 0.65 0.31 0.31 0.06 0.06 SI 0.65 1.29 0.63 0.62

TABLE 11 (CONT)

<u>Use Level</u>	Organism	Q _a _	o _b	O _A	Q _B	si
0.20%	SA	200	1600	10	1990	1.29
tt	ECOLI	100	800	10	1990	2.59
11	PSA	1200	1600	10	1990	1.25
11	PC	1800	1600	10	1990	1.25
tt	CAN	100	16000	10	1990	0.22
11	AN	100	16000	10	1990	0.22

Use Level	Organism	Q _a	Q _b	O _A	O _B	SI
0.40%	SA	200	1600	20	3980	2.59
**	ECOLI	100	800	20	3980	5.18
11	PSA	1200	1600	20	3980	2.50
11	PC	1800	1600	20	3980	2.50
11	CAN	100	16000	20	3980	0.45
11	AN	100	16000	20	3980	0.45

<u>Use Level</u>	Organism	O _a	Q _b	O _A	Q _B	SI	
0.50%	SA	200	1600	25	4975	3.23	
11	ECOLI	100	800	25	4975	6.47	
Ħ	PSA	1200	1600	25	4975	3.13	
er .	PC	1800	1600	25	4975	3.12	
11	CAN	100	16000	25	4975	0.56	
ti	AN	100	16000	25	4975	0.56	

TABLE 12
100:1 Wt. Ratio DMDMH/IPBC

<u>Use Level</u>	Organism	Q _a	O _b	Q _A	O _B	sı
0.01%	SA	200	1600	1	99	0.07
81	ECOLI	100	800	1	99	0.13
11	PSA	1200	1600	1	99	0.06
Ħ	PC	1800	1600	1	99	0.06
11	CAN	100	16000	1	99	0.02
11	AN	100	16000	1	99	0.02
<u>Use Level</u>	Organism	O _a _	O _b	O _A	O _B	SI
0.025%	SA	200	1600	2.5	248	0.17
ti .	ECOLI	100	800	2.5	248	0.33
ti	PSA	1200	1600	2.5	248	0.16
11	PC	1800	1600	2.5	248	0.16
11	CAN	100	16000	2.5	248	0.04
11	AN	100	16000	2.5	248	0.04
Han Invol	Ovenier	•	^	0	0	CT
Use Level	Organism	Q _a _	0 _b	O _A	O _B	SI
0.05% "	SA	200	1600	5	495	0.33
	ECOLI	100	800	5	495	0.67
18	PSA	1200	1600	5	495	0.31
*1	PC	1800	1600	5	495	0.31
11	CAN	100	16000	5	495	0.08
41	AN	100	16000	5	495	0.08

TABLE 12 (CONT)

<u>Use Level</u>	Organism	O _a _	O _b	O _A	Q _B	SI	
0.10%	SA	200	1600	10	990	0.67	
**	ECOLI	100	800	10	990	1.34	
**	PSA	1200	1600	10	990	0.63	
81	PC	1800	1600	10	990	0.62	
11	CAN	100	16000	10	990	0.16	
11	AN	100	16000	10	990	0.16	
Use Level	Organism	O _a _	Q _b	O _A	O _B	SI	
0.20%	SA	200	1600	20	1980	1.34	
t f	ECOLI	100	800	20	1980	2.68	
Ħ	PSA	1200	1600	20	1980	1.25	
11	PC	1800	1600	20	1980	1.25	
11	CAN	100	16000	20	1980	0.32	
11	AN	100	16000	20	1980	0.32	
Use Level	Organism	O _a _	Q _b	O _A	O _B	SI	_
0.40%	SA	200	1600	40	3960	2.68	
11	ECOLI	100	800	40	3960	5.35	
**	PSA	1200	1600	40	3960	2.51	
11	PC	1800	1600	40	3960	2.50	
11	CAN	100	16000	40	3960	0.65	
††	AN	100	16000	40	3960	0.65	
<u>Use Level</u>	Organism	O _a	O _b	O _A	O _B	SI	_
0.50%	SA	200	1600	50	4950	3.34	
11	ECOLI	100	800	50	4950	6.69	
11	PSA	1200	1600	50	4950	3.14	
61	PC	1800	1600	50	4950	3.12	
11	CAN	100	16000	50	4950	0.81	
***	AN	100	16000	50	4950	0.81	

TABLE 13
50:1 Wt. Ratio DMDMH/IPBC

<u>Use Level</u>	Organism	O _a	O _b	<u> </u>	O _B	SI
0.01%	SA	200	1600	2	98	0.07
tī	ECOLI	100	800	2	98	0.14
ır	PSA	1200	1600	2	98	0.06
tr	PC	1800	1600	2	98	0.06
11	CAN	100	16000	2	98	0.03
11	AN	100	16000	2	98	0.03

<u>Use Level</u>	Organism	Q _a .	Q _b	Q _A	Q _B	SI	
0.025%	SA	200	1600	5	245	0.18	
tt	ECOLI	100	800	5	245	0.36	
11	PSA	1200	1600	5	245	0.16	
**	PC	1800	1600	5	245	0.16	
F1	CAN	100	16000	5	245	0.07	
ti	AN	100	16000	5	245	0.07	

<u>Use Level</u>	Organism	Q_a	o _b	Q _A	Q _B	SI_	_
0.05%	SA	200	1600	10	490	0.36	
11	ECOLI	100	800	10	490	0.71	
ŧi	PSA	1200	1600	10	490	0.31	
tī .	PC	1800	1600	10	490	0.31	
11	CAN	100	16000	10	490	0.13	
11	AN	100	16000	10	490	0.13	

TABLE 13 (CONT)

Use Level	Organism	O _a	Q _b	Q _A	Q _B	SI
0.10%	SA	200	1600	20	980	0.71
et	ECOLI	100	800	20	980	1.43
tt	PSA	1200	1600	20	980	0.63
**	PC	1800	1600	20	980	0.62
11	CAN	100	16000	20	980	0.26
11	AN	100	16000	20	980	0.26
<u>Use Level</u>	Organism	Q _a .	Q _b	O _A	O _B	SI
0.20%	SA	200	1600	40	1960	1.43
e1	ECOLI	100	800	40	1960	2.85
88	PSA	1200	1600	40	1960	1.26
**	PC	1800	1600	40	1960	1.25
11	CAN	100	16000	40	1960	0.52
11	AN	100	16000	40	1960	0.52
<u>Use Level</u>	Organism	Q _a	<u> </u>	O _A	O_B	SI
0.40%	SA	200	1600	80	3920	2.85
11	ECOLI	100	800	80	3920	5.70
11	PSA	1200	1600	80	3920	2.52
11	PC	1800	1600	80	3920	2.49
**	CAN	100	16000	80	3920	1.05
11	AN	100	16000	80	3920	1.05
_						
Use Level	-	O _a _	O _b	O _A	Q _B	SI
0.50%	SA	200	1600	100	4900	3.56
11	ECOLI	100	800	100	4900	7.13
11	PSA	1200	1600	100	4900	3.15
**	PC	1800	1600	100	4900	3.12
11	CAN	100	16000	100	4900	1.31
II .	AN	100	16000	100	4900	1.31

TABLE 14
20:1 Wt, Ratio DMDMH/IPBC

<u>Use Level</u>	Organism	O _a	O _b	O _A	O _B	SI
0.01%	SA	200	1600	5	95	0.08
n .	ECOLI	100	800	5	95	0.17
11	PSA	1200	1600	5	95	0.06
•	PC	1800	1600	5	95	0.06
**	CAN	100	16000	5	95	0.06
91	AN	100	16000	5	95	0.06
<u>Use Level</u>	Organism	O _a _	Q _b	O _A	Q _B	sī
0.025%	SA	200	1600	12.5	237.5	0.21
11	ECOLI	100	800	12.5	237.5	0.42
81	PSA	1200	1600	12.5	237.5	0.16
81	PC	1800	1600	12.5	237.5	0.16
81	CAN	100	16000	12.5	237.5	0.14
11	AN	100	16000	12.5	237.5	0.14
<u>Use</u> Level	Organism	Q _a _	O _b	O _A	O_B	SI
0.05%	SA	200	1600	25	475	0.42
**	ECOLI	100	800	25	475	0.84
Ħ	PSA	1200	1600	25	475	0.32
11	PC	1800	1600	25	475	0.31
11	CAN	100	16000	25	475	0.28
71	AN	100	16000	25	475	0.28
Use Level	Organism	Q _a _	O _b	Q _A	OB	SI
0.10%	SA	200	1600	50	950	0.84
n	ECOLI	100	800	50	950	1.69
11	PSA	1200	1600	50	950	0.64
11	PC	1800	1600	50	950	0.62
F1	CAN	100	16000	F 0	OF O	0 E C
tt .	AN	100 100	16000	50	950	0.56 0.56

TABLE 14 (CONT)

Use Level	Organism	O _a	O _b	O _A	O _B	SI
0.20%	SA	200	1600	100	1900	1.69
FF .	ECOLI	100	800	100	1900	3.38
11	PSA	1200	1600	100	1900	1.27
f1	PC	1800	1600	100	1900	1.24
**	CAN	100	16000	100	1900	1.12
11	AN	100	16000	100	1900	1.12
	_	_				
<u>Use Level</u>		<u>Q</u> a_	<u>Q</u> b	Q _A	Q _B	SI
0.40%	SA	200	1600	200	4800	4.00
11	ECOLI	100	800	200	4800	8.00
**	PSA	1200	1600	200	4800	3.17
11	PC	1800	1600	200	4800	3.11
tr	CAN	100	16000	200	4800	2.30
11	AN	100	16000	200	4800	2.30
<u>Use Level</u>	Organism	Q _a _	Q _b	<u>O</u>	O _B	SI_
0.50%	SA	200	1600	250	4750	4.22
11	ECOLI	100	800	250	4750	8.44
11	PSA	1200	1600	250	4750	3.18
11	PC	1800	1600	250	4750	3.11
11	CAN	100	16000	250	4750	2.80
11	AN	100	16000	250	4750	2.80

Similar SI results also were found with GADM and SUTTOCIDE® A as the methylol compound in place of Germall® II or DMDMH in admixtures with IPBC over the same wt. ratios and use level ranges as shown in the Tables 1-14 above.

Tables 1 through 14 above illustrate the synergism of IPBC (compound B) with Germall® II or DMDMH (compound A) at weight ratios of A:B of 2000:1, 1000:1, 500:1, 200:1, 100:1, 50:1 and 20:1. Synergism is very effective for all ratios at low use levels, e.g. 0.01% to 0.1%, against all tested gram-positive, gram-negative organisms and fungi organisms. At slightly higher use concentrations, e.g. 0.20 to 0.50%, all tested ratios were synergistic against Candida albicans and A. niger also. However, at 50:1 and 20:1 ratios, the synergistic effect is negligible at the 0.01 to 0.1% use levels, and non-synergistic even against Candida albicans and A. niger at use levels of 0.20 to 0.50%.

The SI values were lower for Germall® II as the methylol compound in the admixtures as compared to DMDMH.

Similar results were obtained when iodopropynyl alcohol (IPGA) was substituted for IPBC in the admixtures described above.

3. PRESERVATIVE ACTIVITY (CHALLENGE TEST)

A typical cosmetic emulsion was prepared for microbiological challenge testing and predetermined admixtures of a methylol compound and IPBC were added at various use levels. The emulsion thus prepared had the following composition:

Phase A	₹ wt.
Stearic Acid	5.00
Mineral Oil	2.50
Cetyl Alcohol	1.00
Lareth-5 and Ceteth-5 and	
Oleth-5 and Steareth-5	0.50
Glycerol Monostearate and	
Polyoxyethylene Stearate	1.50

Phase B

Deionized Water 88.0 Triethanolamine 99% 1.00

Citric Acid 30% aqueous solution 0.60

Preservative Admixture qs

To prepare the emulsion, Phases A and B were heated separately to 75-80°C. Phase A then was added to Phase B with mixing. The mixture then was cooled to 55-60°C. At this point the desired amount of the preservative admixture was added and the product was cooled to 50°C. while stirring. The citric acid solution then was added to adjust the pH and the mixture was stirred until a temperature of 30°C. was reached.

The challenge tests were carried out using the following microorganisms: SA, ECOLI, PSA, PC, AN and CAN, in this manner. 50 g. aliquots of the test emulsion containing various amounts of the preservative admixture were inoculated with approximately 107-108 of the challenge organisms. The test samples then were stirred to disperse the challenge inoculum. The samples were incubated and assayed at 48 hours, 7, 14, 21 and 28 days. The assays were performed on 1 g. of the test sample by serially diluting 101 to 106 of the original concentration. The plating medium for bacteria was Letheen agar and for fungi it was low pH Mycophil agar with Tween 20. Each plated sample was incubated for 48 hours at 37°C. for bacteria, 5 days at 25°C. for mold, and 3 days at 25°C. for fungi. After incubation, readings of the number of colonies per milliliter (cfu/ml) were made. At 21 days the test product was reinoculated with half of the original inoculum. data is presented in Tables 15-23 below.

15	
3LE	
TABL	

		CEDATIES IT / IDEA	I/IPBC		
	2000	T STOWNS T			
Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
-	000'69	260,000	190,000	17,000	4,500
N	000'86	76,000	1,400	3,100	19,000
COLI	110,000	290,000	2,400	138,000	260,000
	<10	<10	<10	<10	<10
SA	<10	<10	<10	<10	<10
⋖ !	190,000	220	<10	<10	3,700
rganism	48 Hours	7 Days	14 Days	21 Days	28 Days
.	2,800	10	10	<10	220
A	58,000	29,000	18,000	26,000	110,000
COLI	39,000	10	<10	<10	<10
υ	<10	<10	<10	<10	<10
SA	<10	<10	<10	<10	<10
æ	37,000	170	<10	<10	<10
rganism	48 Hours	7 Days	14 Days	21 Days	28 Days
z	20	<10	<10	<10	<10
AN	19,000	6,600	70	<10	320
COLI	3,400	<10	<10	<10	<10
ပ	<10	<10	<10	<10	<10
SA	<10	<10	<10	<10	<10
Ą	31,000	<10	<10	<10	<10
TOUR BELOVE HERVOUS	A Soli Ganism OLI OLI Soli	CAN 98,000 ECOLI 110,000 PC <10	98,000 76,00110,000 290,0010 290,000 290,000 29,000 29,000 39,000 29,000 29,000 20 19,000 6,000 31,000 31,000 31,000	98,000 76,000 1,4 110,000 290,000 2,4 <10 <10 <10 <10 <10 <10 <10 <10 <10 <10	98,000 76,000 1,400 3,7 110,000 290,000 2,400 138,0 <10

		5-4	TABLE 15 (CONT)	(T)			
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days		28 Days
0.1%	AN	<10	<10	<10	∇	<10	<10
=	CAN	180	<10	<10	⊽	<10	<10
Ξ	ECOLI	<10	<10	<10	V	<10	<10
=	PC	<10	<10	<10	V	<10	<10
=	PSA	<10	<10	<10	V	<10	<10
=	SA	750	<10	<10	V	<10	<10
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days		28 Days
0.2%	AN	<10	<10	<10	V	<10	<10
z.	CAN	<10	<10	<10	V	<10	<10
=	ECOLI	<10	<10	<10	V	<10	<10
=	PC	<10	<10	<10	V	<10	<10
=	PSA	<10	<10	<10	v	<10	<10
=	SA	<10	<10	<10	V	<10	<10
Impresented control	100						
חוות	CO11CT O7	1	6				
Organism	48 Hours	7 Days	14 Days	21 Days		28 Days	
AN	52,000	27,000	19,000		19,000	19,000	
CAN	110,000	130,000	240,000		180,000	240,000	
ECOLI	54,000	140,000	170,000		000,	74,000	
PC	6,400,000	6,400,000	2,000,000	9	6,700,000	29,000	
PSA	110,000	700	110,000		290,000	85,000	
SA	2,800,000	250,000	51,000	0	3,700	330	

ABLE 15 (CONT)

Inoculum Concentration	ration	
Organism	0 Hours	21 Days
AN	26,000	53,000
CAN	1,000,000	1,900,000
ECOLI	3,600,000	170,000
PC	3,400,000	87,000
PSA	4,500,000	390,000
SA	4,100,000	200,000

ABLE 16

1000:1 GERMALL® II/IPBC

•			-	O VI	Dued 10	28 Dave
Test Level	<u>Organism</u>	48 HOULS	/ Days	14 Days	21 Day 3	60 Day 08
0.01%	AN	34,000	3,500	80	10	<10
=	CAN	420,000	24,000	950	6,400	6,400,000
=	ECOLI	120,000	63,000	93,000	92,000	000'009'6
=	PC	10	25,000	1,600	15,800	33,000,000
=	PSA	<10	<10	<10	<10	<10
ŧ	SA	100,000	1,400	<10	<10	5,000

TABLE 16 (CONT)

Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.025%	AN	530	10	<10	<10	<10
=	CAN	34,000	750	10	770	240,000
E	ECOLI	120,000	<10	<10	<10	<10
=	- Da	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	37,000	170	<10	<10	<10
			í I			oc oc
Test Level	Organism	48 Hours	7 Days		<u>21 Days</u>	07
0.05%	AN	<10	<10		<10	
=	CAN	13,000	<10		<10	
=	ECOLI	000'89	<10		<10	<10
=	PC	<10	<10		<10	
=	PSA	<10	<10		<10	
=	SA	21,000	<10	<10	<10	
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.1%	AN	<10	<10	<10	<10	<10
=	CAN	10	<10	<10	<10	<10
=	ECOLI	<10	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	1,400	<10	<10	<10	<10

TABLE 16 (CONT)

Test Level	Organism	48 Hours	7_Days	14 Days	21 Days	28 Days
0.2%	AN	<10	<10	<10	<10	<10
=	CAN	<10	<10	<10	<10	<10
=	ECOLI	<10	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
z	PSA	<10	<10	<10	<10	<10
E	SA	<10	<10	<10	<10	<10
Unpreserved control	control					
Organism	48 Hours	7 Days	14 Days	21 Days	28 Days	
AN	52,000	27,000	19,000	19,000		00
CAN	110,000	130,000	240,000		•	00
ECOLI	54,000	140,000	170,000			00
PC	6,400,000	6,400,000	2,000,000	6,700,000	0 29,000	00
PSA	110,000	100	110,000	290,000	0 85,000	00
SA	2,800,000	250,000	51,000	3,700	0 330	0
Inoculum Concentration	centration					
Organism		0 Hours	21 Days			
AN		26,000	53,000			
CAN	1,	1,000,000	1,900,000			
ECOLI	3,	3,600,000	170,000			
PC	3,	3,400,000	87,000			
PSA	4.	4,500,000	390,000			
SA	4,	4,100,000	200,000			

TABLE 17

		500:	500:1 GERMALL® II/IPBC	L/IPBC		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.01%	AN	23,000	40	<10	<10	<10
=		170,000	5,600	290	200	<10
=	ECOLI	000,06	57,000	95,000	70,000	240,000
=	PC	10	<10	<10	>10,000	42,000,000
=	PSA	<10	<10	<10	<10	<10
=	SA	380,000	440	<10	<10	5,100
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	<10	<10	<10	<10	<10
=	CAN	8,700	<10	<10	<10	<10
=	ECOLI	000'09	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	31,000	<10	<10	<10	<10
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.1%	AN	<10	<10	<10	<10	<10
=	CAN	<10	<10	<10	<10	<10
=	ECOLI	<10	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	890	<10	<10	<10	<10

ABLE 17 (CONT)

28 Days	<10	<10	<10	<10	<10	<10			0	0	0	0	00									
21 Days	<10	<10	<10	<10	<10	<10		28 Days	11,000	64,000	120,000	000'009'6	>100,000	<10								
21								21 Days	2,000	12,000	350,000	2,720,000	4,100	220								
14 Days	<10	<10	<10	<10	<10	<10		21														
7 Days	<10	<10	<10	<10	<10	<10		14 Days	18,000	95,000	610,000	3,600,000	130	1,000		21 Days	4,700,000	16,000,000	1,480,000	1,380,000	730,000	360,000
48 Hours	<10	<10	<10	<10	<10	<10		7 Days	520,000	710,000	6,200,000	160,000,000	006	000,009		0 Hours	19,000	340,000	3,900,000	3,800,000	9,200,000	4,800,000
Organism	AN	CAN	ECOLI	PC	PSA	SA	control	48 Hours	6,100	1,000,000	7,100,000	14,600,000	20	43,000,000	ncentration				3,	3,	6	4
Test Level	0.28	=	=	=	=	=	Unpreserved control	Organism	AN	CAN	ECOLI	PC	PSA	SA	Inoculum Concentration	Organism	AN	CAN	ECOLI	PC	PSA	SA

18	
TABLE	

		200:	200:1 GERMALL® II/IPBC	L/IPBC		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.01%	AN	47,000	320	10	<10	<10
=	CAN	810,000	450,000	410,000	190,000	63,000
=	ECOLI	220,000	7,600	<10	850	>1,000,000
=	Dd	10,000	500,000	1,900,000	1,100,000	193,000
z	PSA	<10	<10	<10	<10	<10
=	SA	190,000	23,000	120	<10	<10
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	<10	<10	<10	<10	<10
=	CAN	190	<10	<10	<10	<10
=	ECOLI	37,000	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	19,000	<10	<10	<10	<10
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.18	AN	<10	<10	<10	<10	<10
=	CAN	10	<10	<10	<10	<10
=	ECOLI	<10	<10	<10	<10	<10
I.	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
z	SA	45,000	<10	<10	<10	<10

TABLE 18 (CONT)

28 Days	<10	<10	7	01,	01>	<10	0T>	מ		16,000	640,000	68,000	000,	34,000	750								
21 Days	<10	<10	7	01>	<10	<10	<10	EVER 80	20 03		Đ	•	2,7										
14 Days	<10	01/) /	<10	<10	<10	<10		ZI Days	16,000	590,000	000,066	>10,000	>10,000	580								
7 Days 1	<10	1 7	01>	<10	<10	<10	<10		14 Days	22,000	430,000	410,000	7,000,000	200,000	11,000		21 Days	32,000	1,100,000	1,300,000	3,000,000	4,900,000	2,000,000
48 Hours	/10	0 !	<10	<10	<10	<10	<10		7 Days	32,000	670,000	360,000	3,200,000	9,400	190,000		0 Hours	41,000	640	5,800,000	000,006	1,800,000	7,200,000
, s	Ordanisting.	AN	CAN	ECOLI	D d	PSA	SA	control	48 Hours	89,000	210,000	640,000	19,000,000	80	6,300,000	ncentration				5,		1,	1,7
1	Test Level	0.2%	=	=	=	=	=	Unpreserved control	Organism	AN	CAN	ECOLI	PC PC	PSA	SA	Inoculum Concentration	Organism	AN	CAN	ECOLI	PC PC	PSA	SA

			TABLE 19			
: -		50:	50:1 GERMALL® II/IPBC	I/IPBC		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Davs
*T0.0	AN	4,100	40	<10	<10	<10
: :	CAN	310,000	7,700	560	2,600	5.200
: <u>:</u>	ECOLI	170,000	710	10	<10	120
: =	PG (7,400	74,000	340,000	720,000	520,000
	PSA	<10	<10	<10	<10	30
	SA	110,000	11,000	<10	<10	9,200
Test Level	Organism	48 Hours	7 Dave			
0.05%	AN		7 200	T4 Days	21 Days	28 Days
=	N. C	01>	100	<10	<10	<10
=	CAIN	210	<10	<10	<10	<10
: :	ECOLI	150,000	<10	<10	<10	<10
: s	PC	<10	<10	<10	<10	<10
: :	PSA	<10	<10	<10	<10	(±0)
·	SA	35,000	<10	<10	<10	<10
Test Level	Organism	48 HOUTE	r t	,		
0.1%	3.11	STROTT	/ Days	14 Days	21 Days	28 Days
	AN.	<10	<10	<10	<10	<10
: :	CAN	<10	<10	<10	<10) [V
: :	ECOLI	510	<10	<10	<10	7.0
= :	PG D	<10	<10	<10	010	\T0
: :	PSA	<10	<10	<10	\$1.0 \$1.0	7.00
:	SA	3,000	<10	<10	<10	\10 <10

PABLE 19 (CONT

28 Days	<10	<10	<10	<10	<10	<10		<u>ivs</u>	16,000	640,000	68,000	000,	34,000	120								
21 Days	<10	<10	<10	<10	<10	<10		28 Days	16	640	89	2,760,000	34									
	0	0	0	0	0	0		21 Days	16,000	290,000	000'066	>10,000	>10,000	580								
14 Days	<10	<10	<10	<10	<10	<10		7														
7 Days	<10	<10	<10	<10	<10	<10		14 Days	22,000	430,000	410,000	7,000,000	200,000	11,000		21 Days	32,000	1,100,000	1,300,000	3,000,000	4,900,000	2,000,000
48 Hours	<10	<10	<10	<10	<10	<10		7 Days	32,000	670,000	360,000	3,200,000	9,400	190,000		0 Hours	41,000	640	5,800,000	000,000	1,800,000	7,200,000
Organism	AN	CAN	ECOLI	PC	PSA	SA	control	48 Hours	89,000	210,000	640,000	19,000,000	80	6,300,000	ncentration	5			5,6	•	1,	7,
Test Level	0.2%	=	=	=	Ξ	=	Unpreserved control	Organism	AN	CAN	ECOLI	PC	PSA	SA	Inoculum Concentration	Organism	AN	CAN	ECOLI	PC	PSA	SA

TABLE 20

		20	20:1 GERMALL® II/IPBC	L/IPBC		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.01%	AN	3,100	<10	<10	<10	<10
:	CAN	75,000	220	<10	<10	2,400
=	ECOLI	160,000	110	<10	<10	20
2	PC	12,000	1,000,000	2,100,000	>1,000,000	730,000
=	PSA	<10	<10	<10	<10	4,000
=	SA	140,000	4,100	<10	<10	1,680
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	<10	<10	<10	<10	<10
=	CAN	<10	<10	<10	<10	<10
=	ECOLI	16,000	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10		<10	<10
=	SA	31,000	<10	<10	<10	<10
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.1%	AN	<10	<10	<10	<10	<10
:	CAN	<10	<10	<10	<10	<10
=	ECOLI	<10	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	6,800	<10	<10	<10	<10

3LE 20 (CONT)

28 Days	<10	<10	<10	<10	<10	<10																
21 Days 28	<10	<10	<10	<10	<10	<10		28 Days	16,000	640,000	000'89	2,760,000	34,000	120								
14 Days	<10	<10	<10	<10	<10	<10		21 Days	16,000	230,000	000'066	>10,000	>10,000	580								
7 Days	<10	<10	<10	<10	<10	<10		14 Days	22,000	430,000	410,000	7,000,000	200,000	11,000		21 Days	32,000	1,100,000	1,300,000	3,000,000	4,900,000	2,000,000
48 Hours	<10	<10	<10	<10	<10	<10		7 Days	32,000	670,000	360,000	3,200,000	9,400	190,000		0 Hours	41,000	640	5,800,000	000,000	1,800,000	7,200,000
Organism	AN	CAN	ECOLI	PC	PSA	SA	control	48 Hours	000'68	210,000	640,000	19,000,000	80	6,300,000	<u>ncentration</u>				5,		' T	12
Test Level	0.2%	=	=	z	Ξ	*	Unpreserved control	Organism	AN	CAN	ECOLI	PC	PSA	SA	Inoculum Concentration	Organism	AN	CAN	ECOLI	PC	PSA	SA

	/IPBC
TABLE 21	DMDMH/
TA	1
	2000

		(0)	2000:1 DMDMH/IPBC	PBC		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.025%	AN	4,100	38,000	270	80	100
=	CAN	270,000	1,900,000	550,000	220,000	210,000
=	ECOLI	1,300,000	<10	<10	<10	3,000
=	PC	<10	<10	<10	<10	<10
E	PSA	<10	<10	<10	<10	<10
=	SA	42,000	20	<10	<10	<10
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	<10	<10	<10	<10	<10
=	CAN	770,000	130,000	670,000	160,000	64,000
=	ECOLI	220,000	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
*	SA	000'6	<10	<10	<10	<10
					,	
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
	AN	<10	<10	<10	<10	<10
	CAN	580	840	500	40,000	83,000
=	ECOLI	340	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	29,000	<10	<10	<10	<10

TABLE 21 (CONT)

28 Days	<10	21	<10	<10	<10	<10			00	00	000	000	000	110								
21 Days	<10	<10	<10	<10	<10	<10		28 Days	6,000	790,000	140,000	31,000,000	300,000	Ħ								
21								21 Days	5,200	480,000	240,000	8,500,000	15,200	3,000								
14 Days	<10	10	<10	<10	<10	<10		21				80										
7 Days	<10	10	<10	<10	<10	<10		14 Days	24,000	3,300,000	7,300,000	2,900,000	100	12,000		21 Days	41,000	640	5,800,000	000,006	000'000'6	7,200,000
48 Hours	<10	<10	<10	<10	<10	<10		7 Days	36,000	1,	2,500,000	15,600,000	<10	>1,000,000		0 Hours	20,000	1,400,000	4,800,000	9,200,000	000'006'9	5,700,000
Organism	AN	NAC	ECOLI)))	PSA	SA	control	48 Hours	37,000	120,000	150,000	19,000,000	<10	SA 7,000,000	centration			1	4	6	9	ស
Test Level	0.28		=	=	=	=	Unpreserved control	Organism			ij			SA	Inoculum Col	Organism	AN	CAN	ECOLI	PC	PSA	SA

	IPBC
22	
띡	/HWQWQ
TABI	1 D
- '	00

			TABLE 22			
		[1000:1 DMDMH/IPBC	IPBC		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.025%	AN	650	006	<10	<10	140
=	CAN	000'16	000'006	2,300,000	120,000	120,000
=	ECOLI	160,000	<10	<10	<10	2,400
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	23,000	<10	<10	<10	06
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	20	<10	<10	<10	<10
=	CAN	65,000	520,000	26,000	32,000	370,000
=	ECOLI	26,000	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	12,000	<10	<10	<10	<10
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.1%	AN	<10	<10	<10	<10	<10
=	CAN	3,100	4,800	180	640	4,400
=	ECOLI	45,000	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	6,000	<10	<10	<10	<10

CABLE 22 (CONT)

Test Level	Organism	48 Hours	7 Days	14 Days 21	21 Days 28	28 Days
0.2%	AN	<10	<10	<10	<10	<10
=	CAN	<10	<10	<10	<10	<10
=	ECOLI	<10	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
z	SA	180	<10	<10	<10	<10
Unpreserved control	control					
Organism	48 Hours	7_Days	14 Days	21 Days	28 Days	
AN	37,000	36,000	24,000	5,200	000'9	
CAN	120,000	1,900,000	3,300,000	480,000	790,000	
ECOLI	150,000	2,500,000	7,300,000	240,000	140,000	
PC	19,000,000	15,600,000	5,900,000	8,500,000	31,000,000	
PSA	<10	<10	100	15,200	300,000	
SA	7,000,000	>1,000,000	12,000	3,000	110	
Inoculum Concentration	centration					
Organism		0 Hours	21 Days			
AN		50,000	41,000			
CAN	1	1,400,000	640			
ECOLI	4	4,800,000	5,800,000			
PC	6	9,200,000	000'006			
PSA	9	6,900,000	000,000,6			
SA	ហ	5,700,000	7,200,000			

TABLE 23	1 GADM/IPBC
TABI	000:1

			C2 70000			
			2000:1 GADM/IPBC	PBC		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.025%	AN	300	21	10	<10	11
=	CAN	480,000	890,000	940,000	1,040,000	130,000
=	ECOLI	230,000	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	78,000	<10	<10	<10	<10
Test Level	<u>Organism</u>	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	<10	<10	<10	<10	<10
=	CAN	110,000	4,100,000	3,600,000	330,000	97,000
=	ECOLI	120,000	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
	SA	56,000	<10	<10	<10	<10
Test Level	<u>Organism</u>	48 Hours	7 Days	14 Days	21 Days	28 Days
0.1%	AN	<10	<10	<10	<10	<10
=	CAN	1,200,000	53,000	430,000	144,000	110,000
=	ECOLI	<10	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	<10	<10	<10	<10	<10

FABLE 23 (CONT

28 Days	<10	09	<10	<10	<10	<10			0	0	0	0	0									
21 Days	<10	<10	<10	<10	<10	<10		28 Days	5,400	170,000	140,000	1,400,000	100,000	80								
	0	0	0	0	0	0.		21 Days	13,000	200,000	920,000	10,000,000	12,800	7,100								
14 Days	<10	<10	<10	<10	<10	<10		(2)														
7 Days	<10	<10	<10	<10	<10	<10		14 Days	33,000	780,000	920,000	10,000,000	12,800	7,100		21 Days	10,000	310,000	3,500,000	2,500,000	5,400,000	4,100,000
48 Hours	<10	000,06	<10	<10	<10	<10		7 Days	33,000	780,000	3,100,000	30,000,000	009	410,000		0 Hours	53,000	1,900,000	170,000	87,000	390,000	200,000
Organism	AN	CAN	ECOLI	PC	PSA	SA	control	48 Hours	50,000	780,000	000,009	11,000,000	3,800	14,000,000	ncentration			1,				
Test Level	0.28	; =	=	=	=	I	Unpreserved control	Organism	AN	CAN	ECOLI	PC	PSA	SA	Inoculum Concentration	Organism	AN	CAN	ECOLI	PC	PSA	SA

Discussion of Challenge Testing Results

The 28-day challenge results reported in Tables 15-23 above demonstrate the effectiveness of the preservative admixture of the invention in a use emulsion composition against a wide range of bacteria and fungi organisms.

For example, admixture compositions of Germall® II and IPBC at a wt. ratio of 2000:1 (Table 15), when present at use levels of 0.05 to 0.2%, corresponding to 0.75 to 10 ppm IPBC and 500 to 2000 ppm methylol levels, provide substantially complete protection against all tested organisms after 28 days. At the low use level of 0.05% active, all the challenge tests passed within 21 days. Then, upon reinoculation after 21 days, all organisms died within 7 days except CAN which cleared within 14 days.

Table 21 shows the challenge test results for DMDMH and IPBC admixtures at the same 2000:1 wt. ratio. A use level of 0.2%, however, is needed for this blend to pass against all organisms after 21 days. Upon reinoculation, all organisms died within 7 days with the exception of CAN which cleared within 14 days. It is thus evident from these results that Germall® II blended with IPBC is 4 times more effective than a DMDMH/IPBC blend.

Germall® II also is superior to GADM as the methylol compound, as shown in Table 23.

Table 24 below is a study of the activity of solution of GII/IPBC in propylene glycol. The admixtures of the active GII and IPBC components were prepared at weight ratios of 99.5%/0.5% and 99%/1%, and added to 60% by weight propylene glycol. The resulting solutions were tested at 0.05%, 0.1% and 0.2% total active in a proteinaceous shampoo formulation.

TABLE 2

99.5% GII/0.5	% IPBC/propyl	99.5% GII/0.5% IPBC/propylene glycol solution - 0.05% total active	ion - 0.05%	total active		,
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	310,000	2,000	<10	<10	<10
; ;	CAN	44,000	2,400	<10	<10	1,800
=	ECOLI	3,000	<10	<10	<10	<10
E	PC	400,000	62,000	06	<10	>10,000
=	PSA	5,300,000	3,000	<10	<10	>10,000
Ξ	SA	10	10	<10	<10	<10
9 64 511/0/	5% TPBC/probvl	oo s* cii/n s* TPRC/propylene glycol solution - 0.1% total active	ion - 0.1%	total active		
The T.evel	Ordanism	48 Hours	7 Days	14 Days	21 Days	28 Days
18	AN	210,000	<10	<10	<10	<10
, ,	CAN	1,500	<10	<10	<10	<10
Ξ	ECOLI	580	<10	<10	<10	20
E	PC	34,000	<10	<10	<10	<10
=	PSA	780	<10	<10	<10	<10
=	SA	<10	<10	<10	<10	<10

	21 Days 28 Days	<10 <10	<10 <10	<10 <10	<10 <10	<10 <10	<10 <10		21 Days 28 Days		<10 <10			3,	3,	r.	, E	3, 28 D		3 y S	3, 28 D	3, 28 D	3, 28 D
	14 Days	<10	<10	<10	<10	<10	<10	1 active	14 Days		<10	<10	<10 <10 <10	<pre></pre> <pre><10 <10 <10 <10 </pre>	<pre></pre> <pre><</pre>	<pre><10 <10 <10 <10 <10 <10 <10 </pre>	<10 <10 <10 <10 <10 <10	<10 <10 <10 <10 <10 <10 <10	<10 <10 <10 <10 <10 <10 <10 <10	<10 <10 <10 <10 <10 <10 <10 <10 <10	<10 <10 <10 <10 <10 <10 <10 <10 <10	<10 <10 <10 <10 <10 <10 <10 <10 <10 <10	<10 <10 <10 <10 <10 <10 <10 <10 <10 <10
Tipe Table To Table T	7 Days	<10	<10	<10	<10	<10	<10	- 0.05% total	7 Days		<10	<10	<10 <10 <10	<10 <10 <10 <10	<10 <10 <10 <10 <10	<10 <10 <10 <10 <10 <10	0 13	1	1	1	1	1	1
	48 Hours	<10	<10	<10	<10	<10	<10	riycol solution	48 Hours		89,000	89,000	89,000 4,400 3,300	89,000 4,400 3,300 260,000	89,000 4,400 3,300 260,000 64,000	89,000 4,400 3,300 260,000 64,000	89,000 4,400 3,300 260,000 64,000 <10	89,000 4,400 3,300 260,000 64,000 <10 <10	89,000 4,400 3,300 260,000 64,000 <10 <10	89,000 4,400 3,300 260,000 64,000 <10 <10 48 Hours 37,000	89,000 4,400 3,300 260,000 64,000 <10 <10 37,000 <10	89,000 4,400 3,300 260,000 64,000 <10 48 Hours 37,000 840 48,000	89,000 4,400 3,300 260,000 64,000 <10 48 Hours 37,000 10 840 840 48,000
	Organism	AN	CAN	ECOLI	PC	PSA	SA	99% GII/1% IPBC/propylene glycol	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Ordanism	Organism AN	Organism AN CAN	Organism AN CAN ECOLI	Organism AN CAN ECOLI	Organism AN CAN ECOLI PC	Organism AN CAN ECOLI PC PSA	Sest Level Organism 48 hours	Organism AN CAN ECOLI PC PSA SA Organism	Organism AN CAN ECOLI PC PSA SA Organism AN	Organism AN CAN ECOLI PC PSA SA SA Organism AN CAN	Organism AN CAN ECOLI PC PSA SA SA Organism AN CAN ECOLI	Organism AN CAN ECOLI PC PSA SA SA Organism AN CAN ECOLI	Organism AN CAN ECOLI PC PSA SA SA Organism AN CAN ECOLI PC PC
99.5% GII/0.5% IPBC/propylene	Test Level	0.2%	=	=	=	=	=	99% GII/1% IF	Test Level		0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05% " " " " 99% GII/1% I]	0.05% " " " " 29% GII/1% II	0.05% " " " " Test Level 0.1%	0.05% " " " " 29% GII/1% II Test Level 0.1%	0.05% " " " Test Level 0.1% "	0.05% "" "" "" Test Level 0.1% ""	0.05% " " " Test Level 0.1% " "

Test Level Organ	Organism AN CAN ECOLI PSA SA CONTROL 48 HOURS 4,000,000 160,000 >100,000,000 centration 2,	99 & GIL/1 & IPBC/DEOPYIERE 41/OLD 50.2 & AN 48 Hours 7 Days 14 Days 0.2 * AN <10 <10 <1 " CAN <10 <10 <1 " ECOLI <10 <10 <1 " PC <10 <10 <1 " PC <10 <10 <1 " SA <10 <10 <1 Organism 48 Hours 7 Days 14 Days 2 AN 4,000,000 >100,000,000 5,600,000 48 ECOLI >100,000,000 50,000,000 56,000,000 48 ECOLI >100,000,000 50,000,000 58,000,000 58 ECOLI >100,000,000 50,000,000 58,000,000 58 Inoculum Concentration OHOUR 2,100,000 4,200,000 CAN 380,000 5,300,000 5,300,000 CAN 860,000 5,300,000 5,300,000 5,300,000	7 Days <10 <10 <10 <10 <10 <10 <10 <10 <10 <10	0 0 0 0 0 0,000,000 3,000,000 5,000,000	21 Days 22	28 Days <10 <10 <10 <10 <10 <10 <00 <00
PC PSA SA	, t. 5. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2.	1,900,000 3,200,000 2,400,000	60,000,000 5,000,000 3,000,000			

Table 25 shows a similar study as in Table 24 above in which the vehicle for the composition was the typical emulsion described above.

TABLE 2

99.5% GII/0.5% IPBC/propylene glycol solution - 0.05% total active	IPBC/propylen	e qlycol solut	ion - 0.05%	total active		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	40	<10	<10	<10	<10
=	CAN	520,000	<10	<10	<10	<10
=	ECOLI	320	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	24,000	<10	<10	<10	<10
99.5% GII/0.5% IPBC/propylene glycol solution - 0.1% total active	IPBC/propylen	e glycol solut	ion - 0.1%	cotal active		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.1%	AN	<10	<10	<10	<10	<10
=	CAN	<10	<10	<10	<10	<10
=	ECOLI	10	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	A.S.	650	<10	<10	<10	<10

99.5% GII/0.5% IPBC/		propylene glycol solution		0.2% total active		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.2%	AN	<10	<10	<10	<10	<10
	CAN	<10	<10	<10	<10	<10
E	ECOLI	<10	<10	<10	<10	<10
E	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
z	SA	<10	<10	<10	<10	<10
99\$ GII/1\$ Il	PBC/propylene	99% GII/1% IPBC/propylene glycol solution	- 0.05% total active	1 active		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.05%	AN	<10	<10	<10	<10	<10
=	CAN	6,700	<10	<10	<10	<10
=	ECOLI	000'99	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	50,000	<10	<10	<10	<10
99% GII/1% I	PBC/propylene	99% GII/1% IPBC/propylene glycol solution	- 0.1% total	l active		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.1%	AN	<10	<10	<10	<10	<10
=	CAN	<10	<10	<10	<10	<10
•	ECOLI	<10	<10	<10	<10	<10
=	PC	<10	<10	<10	<10	<10
=	PSA	<10	<10	<10	<10	<10
=	SA	620	<10	<10	<10	<10

99% GII/1% I	PBC/propylen	99% GII/1% IPBC/propylene glycol solution	n - 0.2% total active	active		
Test Level	Organism	48 Hours	7 Days	14 Days	21 Days	28 Days
0.2%	AN	<10	<10	<10	<10	<10
=	CAN	<10	<10	<10	<10	<10
=	ECOLI	<10	<10	<10	<10	<10
Ξ	PC Dd	<10	<10	<10	<10	<10
5	PSA	<10	<10	<10	<10	<10
=	SA	<10	<10	<10	<10	<10
Unpreserved control	control					
Organism	48 Hours	7 Days	14 Days	21 Days	28 Days	សា
AN	3,100,000	650,000	370,000	1,400,000	260,000	c
CAN	6,000,000	4,000,000	1,100,000	5,800,000	>1,000,000	0
ECOLI	11,000,000	7,300,000	000'000'9	730,000	220,000	o
PC	100,000,000	53,000,000	40,000,000	40,000,000	000,009	0
PSA	5,000,000	200,000	2,700,000	72,000	20,000	0
SA	30,000,000	150,000	440,000	2,500	006'6	0
Inoculum Concentration	centration					
Organism		0 Hours	21 Days			
AN		380,000	330,000			
CAN		860,000	4,200,000			
ECOLI	8	2,500,000	5,300,000			
PC	F	1,900,000	000,000,009			
PSA	6	3,200,000	2,000,000			
SA	N	2,400,000	3,000,000			

The results shown in Tables 24 and 25 demonstrate that the compositions of the invention are completely effective against the tested organisms in comparison to the unpreserved controls.

While the invention has been described with particular reference to certain embodiments thereof, it will be understood that changes and modifications may be made which are within the skill of the art. Accordingly, it is intended to be bound only by the following claims, in which:

WHAT IS CLAIMED IS:

- 1. A water soluble preservative antimicrobial composition for addition to commercial use products at predetermined use levels to provide synergistic biocidal activity against a wide range of fungi and gram-negative and gram-positive bacteria, comprising
 - (1) an admixture of
 - (a) one or more methylol compounds, and
- (b) 3-iodo-2-propynylbutyl carbamate, in a weight ratio of (a):(b) of 100:1 to 2000:1.
- 2. A water soluble preservative admixture according to claim 1 wherein said weight ratio is 200:1 to 500:1.
- 3. A water soluble preservative admixture according to claim 1 wherein
- (a) is N-[1,3-bis(hydroxymethyl)-2,5-dioxo-4-imidazolidinyl]-N,N'-bis(hydroxymethyl) urea, imidurea, 1,3-dimethylol-5,5-dimethyl hydantoin, sodium hydroxymethylglycinate, or glycine anhydride dimethylol.
- 4. A preservative admixture according to claim 3 wherein
- (a) is N-[1,3-bis(hydroxymethyl)-2,5-dioxo-4-imidazolidinyl]-N,N'-bis(hydroxymethyl) urea.
- 5. A composition according to claim 1 which also includes (2) propylene glycol or 1,3-butylene glycol.

- 6. A water soluble preservative antimicrobial composition according to claim 5 which comprises about 20 to 55 weight percent of (1) and 45 to 80 weight percent of (2).
- 7. A composition according to claim 6 which comprises about 40 weight percent of (1) and about 60 weight percent of (2).
- 8. A commercial use product which is protected for an extended period of time against contamination by a wide range of fungi and gram-negative and gram-positive bacteria which includes 0.01 to 0.5% by weight of the water soluble preservative composition of claims 1-7.
- 9. A commercial use product according to claims 1-8 which includes about 0.1% by weight of the water soluble preservative composition of claim 2 or 5.
- 10. A commercial use product according to claims 1-9 in which said composition is water solubilized and uniformly distributed throughout said composition.
- 11. A commercial use product according to claims 1-10 in which (b) is present therein in an amount of 0.5 to 10 ppm, and (a) is present in an amount of at least 250 ppm.

- 12. A commercial use product according to claims 1-11 which is a personal care, household or industrial composition.
- 13. A commercial use product which is protected for an extended period of time against contamination by a wide range of fungi and gram-negative and gram-positive bacteria which includes 0.1 to 5% by weight of the composition of claims 1-12.
- 14. A product according to claim 13 which includes about 0.5 to 1% by weight of the composition of claim 1 or 5.

INTERNATIONAL SEARCH REPORT

International application No. PCT/US95/04895

A. CLA	SSIFICATION OF SUBJECT MATTER	
	Please See Extra Sheet.	
According to	514/252, 389, 390, 478, 479, 561 International Patent Classification (IPC) or to both national classification and IPC	
	DS.SEARCHED	
	ocumentation searched (classification system followed by classification symbols)	
U.S. : 5	514/252, 389, 390, 478, 479, 561	
Documentat	ion searched other than minimum documentation to the extent that such documents are included	in the fields searched
Electronic d	ata base consulted during the international search (name of data base and, where practicable,	search terms used)
C. DOC	UMENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Υ	US, A, 4,844,891 (Rosen et. al.) 04 July 1989, see entire document.	1-14
Y	US, A, 3,987,184 (Foelsch) 19 October 1976, see entire document.	1-3 and 5-14
Υ	US , A, 5,244,653 (Berke et. al.) 14 September 1993, see entire document.	1-3 and 5-14
Υ	US, A, 4,337,269 (Berke et. al.) 29 June 1982, see entire document.	1-3 and 5-14
Υ	US, A, 4,655,815 (Jakubowski) 07 April 1987, see entire document.	1-3 and 5-14
Furti	ner documents are listed in the continuation of Box C. See patent family annex.	161-1-1
	ecial categories of cited documents: tater document published after the int date and not in conflict with the apply in graciple or theory underlying the interpretation of the art which is not considered principle or theory underlying the interpretation.	cation but cited to understand the
to	be of particular relevance "Y" document of particular relevance; the	he claimed invention cannot be
it. do	riser document published on or after the international fitting date considered novel or cannot be considered novel or cannot b	ered to involve an inventive step
ap	ed to establish the publication date of another citation or other ecial reason (as specified) cument referring to an oral disclosure, use, exhibition or other combined with one or more other successful to the combined with th	s step when the document is ch documents, such combination
l m	being obvious to a person skilled in the same patents. **A** document published prior to the international filing date but later than **A** document published prior to the international filing date but later than **A**	the art
th	e priority date claimed actual completion of the international search Date of pulling of the international search	
12 JULY	31.07.95	0
Commission Box PCT	mailing address of the ISA/US oner of Patents and Trademarks on, D.C. 20231 Authorized Office ALEN ROBINSON	allino
Facsimile I	No. (703) 305-3230 Telephone No. (703) 308-1235	- A
Form PCT/	SA/210 (second sheet)(July 1992)*	()

INTERNATIONAL SEARCH REPORT

International application No. PCT/US95/04895

A01N 37/12, 37/44, 43/50, 43/58, 43/60, 47/10; A61K 31/27, 31/50, 31/195, 31/415, 31/495		A. CLASSIFICATION OF SUBJECT MATTER: IPC (6):
		A01N 37/12, 37/44, 43/50, 43/58, 43/60, 47/10; A61K 31/27, 31/50, 31/195, 31/415, 31/495
	,	